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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,068	04/06/2001	Yong-Hwan Moon	18941001400	7267

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,068	MOON ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,10,14,16,20 and 22-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10,14,16,20,22-24 and 26-32* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 7-8, 10, 14, 16, 20, and 22-32 are pending.

Claims 1-6, 9, 11-13, 15, 17-19, and 21 are canceled.

Claims 25-32 are newly added.

2. Claims 7-8, 10, 14, 16, 20, and 22-32 are examined in the present office action.

RCE Acknowledgment

3. The request filed on December 22, 2003 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/828068 is acceptable and a RCE has been established. An action on the RCE follows.

4. The Office contends that in the last office action mailed 8/20/2003, paragraph #3, claims 1-9 and 14-21 were inadvertently reported as being the elected claims. Claims 6, 11, and 17 should have been reported as claims non-elected.

Specification

5. The "Brief Description of the Drawings" is objected to because Applicant has submitted Figures 1A-1H filed 5/19/2003 but the Brief Description of the Drawings only references "Figure 1". The Brief Description of the Drawings should be amended to include Figures 1A-1H.

Claim Objections

6. Claim 16 is objected to for reciting "an amino acid sequence" instead of "the amino acid sequence". For purposes of compact prosecution, the claim is interpreted to mean the amino acid sequence set forth in SEQ ID NO:2.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 7-8, 14, 16, 20, 22-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

In claim 7, line 1, insert the recitation --sequence-- before "identity" to clarify Applicants' claimed invention.

In claim 14, line 5, insert the recitation --sequence-- before "identity" to clarify Applicants' claimed invention.

Claims 14 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: wherein the introduced nucleic acid sequence is transcribed resulting in an earlier flowering time when compared to a plant not transcribing said nucleic acid sequence.

In claim 27, line 2, insert the recitation --sequence-- twice, once after "acid", and again before "identity" to clarify Applicants' claimed invention.

In claim 30, line 1, insert the recitation --sequence-- after "acid" to clarify Applicants' claimed invention.

In claim 30, line 3, insert the recitation --sequence-- twice, once after "acid", and again before "identity" to clarify Applicants' claimed invention.

In claim 31, line 3, insert the recitation --sequence-- twice, once after "acid", and again before "identity" to clarify Applicants' claimed invention.

In claim 32, line 1, insert the recitation --sequence-- after "acid" to clarify Applicants' claimed invention.

Written Description

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 7-8, 14, 20, 23, and 26-27, 29, and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2, or an expression

cassette and plant comprising said sequence, a method of decreasing flowering time in a plant comprising transforming a plant with said sequence, or wherein said sequence comprises a nucleic acid sequence having 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering, an expression cassette comprising a nucleic acid sequence having at least 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering.

Applicants disclose a single nucleotide sequence of SEQ ID NO:1 encoding the rice *Oryza sativa* EMBRYONIC FLOWER1 (OsEMF1) polypeptide sequence of SEQ ID NO:2.

Applicants do not identify essential regions of OsEMF1 protein encoded by SEQ ID NO:1, nor do Applicants describe any polynucleotide sequences encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2, nor any polynucleotide sequences comprising a nucleic acid sequence having at least 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative

number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a OsEMF1 protein, or sequences falling within the scope of the claimed genus that can be used to suppresses gene expression which results in earlier flowering. Applicants only describe a single cDNA sequence of SEQ ID NO:1. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides and structural features common to members of the claimed genus that can be used to suppresses gene expression which results in earlier flowering. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the OsEMF1protein and regions essential to suppress gene expression which results in earlier flowering, it remains unclear what features identify a OsEMF1 protein and what features identity a sequence comprising a nucleotide sequence exhibiting at least 95% sequence identity to 100 contiguous nucleotides of SEQ ID NO:1 that can be used to suppress gene expression which results in earlier flowering. Since the genus of OsEMF1 proteins has not been described by specific structural features, and since the genus of sequences comprising nucleotide sequences exhibiting 95% sequence identity to 100 contiguous nucleotides of SEQ ID NO:1 that can be used to suppress gene expression which results in earlier flowering, has not been described, the specification fails to provide an adequate written description to support the breath of the claims.

Sequences that encode a polypeptide having at least 90% sequence identity to SEQ ID NO:2 encompass naturally occurring allelic variants, mutants of OsEMF1 of SEQ ID NO:2, as well as sequences encoding proteins having no known OsEMF1 activity, of which Applicant is not in possession. Absent of such disclosure, one skilled in the art cannot determine the genus of sequences based upon the disclosure of the sequence of SEQ ID NO:1 encoding SEQ ID NO:2 with any certainty or predictability. Accordingly, the specification fails to provide an adequate written description to support the percent identity language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

In the paper filed 12/22/2003, Applicants contend the written description requirement is fulfilled for claims drawn to sequence exhibiting 95% sequence identity to at least 100 nucleotides of SEQ ID NO:1. Applicants continue by stating that those skilled in the art at the time of filing are capable of identifying any sequence of at least 100 nucleotides within SEQ ID NO:1 and in addition, could easily generate sequences exhibiting 95% sequence identity to such sequences (page 8, last paragraph). Applicants also contend that the recited gene fragments need not encode any active protein, but rather, are only required to have a gene silencing effect (page 9, 1st full paragraph).

The Office contends that the issue at hand is whether Applicants have fulfilled the written description requirement for their broadly claimed invention. Applicants' claims are drawn to DNA sequences which are not described in the specification. In particular, the Federal Circuit stated, "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the

inventor invented the claimed invention." In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The Office asserts that whereas Applicants have describe a nucleic acid sequence comprising the full nucleic acid sequence of SEQ ID NO:1, Applicants have failed to describe any sequence exhibiting 95% sequence identity to 100 contiguous nucleotides of SEQ ID NO:1 and function to suppress gene expression which results in a plant that flowers earlier than a plant not transformed with said sequence. Hence, Applicants have not fulfilled the written description requirement. To satisfy the test set forth in *Eli Lilly,* Applicants need to describe a representative number of sequences encompassed by the claimed genus or structural domains or specific sequence motifs that are required to silence the endogenous gene. As Applicants fail to provide either, it is not clear that Applicants were in possession of the claimed invention at the time of filing, and Applicants fail to satisfy the written description requirement.

Scope of Enablement

9. Claims 7-8, 10, 14, 16, 20, 22-24, and 26-32 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule of SEQ ID NO:1 encoding SEQ ID NO:2, and plant transformed therewith, wherein introduction of the nucleic acid molecule into a plant suppresses gene expression which results in earlier flowering in the plant compared to a plant not transformed, and a method of decreasing

flowering time in a plant comprising said nucleic acid sequence, does not reasonably provide enablement for claims drawn to degenerate DNA, percent identity or 100 contiguous nucleotides of SEQ ID NO:1, plant transformation therewith including methods of decreasing flowering time. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2, or an expression cassette and plant comprising said sequence, a method of decreasing flowering time in a plant comprising transforming a plant with said sequence, or wherein said sequence comprises a nucleic acid sequence having 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering, or wherein said sequence comprises at least 100 contiguous nucleotides of SEQ ID NO:1, an expression cassette comprising a nucleic acid sequence having

at least 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering, or wherein said sequence comprises 100 contiguous nucleotides of SEQ ID NO:1.

Applicants isolated the rice EMBRYONIC FLOWER (EMF1) homolog, OsEMF1, from rice using the rapid amplification of cDNA ends (RACE) technique (page 224, lines 14-18). Applicants do not disclose any of the conditions, nor primers that were used to amplify the corresponding cDNA. In the 37 C.F.R. §1.132 Declaration of Z. Renee Sung, Ph.D. filed 5/19/2003, Applicant asserts that transgenic rice plants were produced comprising UBQ::sense OSEMF 1 which resulted in rice plants flowering earlier than plants not transformed. Applicant asserts that Arabidopsis plants harboring a 35S::sense EMF1 construct also flowered early. Applicant contends that these results indicate that co-suppression of OsEMF1 is also effective to reduce flowering time in a plant (page 2 of Declaration, paragraphs 3-5).

Applicants fail to teach nucleotide sequences encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2, nucleotide sequences having 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1, a nucleic acid sequence comprising at least 100 contiguous nucleotides of SEQ ID NO:1, methods of decreasing flowering time in a plant comprising any of said sequences or a plant transformed therewith.

The claims are broadly drawn to any nucleotide sequence encoding a protein having 90% sequence identity to SEQ ID NO:2, or any nucleotide sequence exhibiting 95% sequence identity to 100 contiguous nucleotides of SEQ ID NO:1. The instant specification fails to provide guidance for which 100 contiguous nucleotides of SEQ ID NO:1 can be used to co-suppress gene

expression, or which sequences exhibiting 95% sequence identity to any 100 contiguous nucleotides of SEQ ID NO:1 can be used to suppress gene expression or which degenerate DNA that includes a nucleotide sequences encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2 can be used to co-suppress a gene. Degenerate DNA used for co-suppression is highly unpredictable.

The state-of-the-art teaches that sense and antisense constructs can behave unpredictably when transformed into a plant. Colliver et al (1997, Plant Mol. Biol. 35:509-522) showed that tranformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase unexpectedly resulted in transformants with *increased* levels of chalcone synthase transcripts (page 519, left column, 2nd paragraph). Montgomery et al (Trends in Genetics, July 1998, 14(7):255-258) teach that not all transgenes can cause co-suppression in plants and that there is no basis for predicting which transgenes would have this effect (page 257, column 1, last paragraph).

The state-of-the-art teaches that strict complementarity is crucial for proper gene silencing involving the antisense or sense gene silencing mechanism. Emery et al (2003, Current Biology 13:1768-1774) disclose experiments in which a target sequence of a micro-RNA was changed by two base-pairs. The altered base-pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence's encoded protein (page 1769, right column, 2nd full paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 as a probe, by designing primers to

undisclosed regions of SEQ ID NO:1 and isolating or amplifying fragments, or by making 100 contiguous base pair sequences by using PCR or by base-pair deletion methodologies, subcloning the fragments into expression vectors and transforming plants therewith, in order to identify those, if any, that encode a protein exhibiting at least 90% sequence identity to SEQ ID NO:2, or sequences that exhibit at least 95% sequence identity to a 100 contiguous nucleotide sequence of SEQ ID NO:1 and when transformed into a plant suppress gene expression which results in early flowering.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

In the paper filed 12/22/2003, Applicants contend that the specification teaches co-suppression in which the sequences are of various lengths and do not have to include the coding sequences and need not have absolute identity (page 6, 4th paragraph). Applicants contend gene fragments will actually suppress gene expression. As an example, Applicants reference the Stam et al (1997, Annals Bot. 79:3-12) reference and cite it as teaching that co-suppression is now frequently used to study gene function (page 7, 1st full paragraph). Applicants argue enablement of co-suppression by citing Waterhouse et al (1998, PNAS 95:13959-13964) which teaches double-stranded RNA that is involved in co-suppression and Singh et al (2000, Biochem Soc Trans. 28(6):925-7) which teaches the use of inverted repeats and/or intronic sequences to optimize co-suppression (page 7, 2nd and 3rd full paragraphs). Lastly, Applicants cite Thomas et al (2001, Plant J. 25(4):417-425) as teaching that as few as 23 nucleotides of complimentary

contiguous sequence was necessary to silence green fluorescent protein in plants (page 8, 1st paragraph).

The Office acknowledges that Applicants' specification teaches co-suppression, but as indicated above, the techniques associated with gene silencing are accompanied by much unpredictability. The Office acknowledges that the Stam et al reference does teaches post-transcriptional gene silencing but, Stam et al also teach that the co-suppression by transgenes does not necessarily occur in all cells. Stam et al state "..silencing does not always occur in every cell of a particular tissue. In the case of anthocyanin gene silencing, this is clearly visible by the various flower coloration patterns (page 6, left column, last paragraph). In addition, Thomas et al teach that not all fragments of a gene will cause co-suppression. Thomas et al teach that not all 20-30 nucleotide fragments of green fluorescent protein (GFP) were capable of silencing GFP that was transformed into tobacco (page 419, Table 1). In response to applicant's argument concerning Waterhouse et al and Singh et al, it is noted that the features upon which applicant relies (i.e., concerning double stranded RNA, inverted repeats and/or intronic sequences) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). And lastly, Applicants disclose that the before mentioned techniques of co-suppression are known in the art, but Applicant has not taught a fragment comprising a sequence exhibiting 95% sequence identity to 100 contiguous nucleotides of SEQ ID NO:1. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not

constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

10. Claims 7-8, 10, 14, 16, 20, and 22-32 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2, or an expression cassette and plant comprising said sequence, a method of decreasing flowering time in a plant comprising transforming a plant with said sequence, or wherein said sequence comprises a nucleic acid sequence having 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering, or wherein said sequence comprises at least 100 contiguous nucleotides of SEQ ID NO:1, an expression cassette comprising a nucleic acid sequence having at least 95% sequence identity to at least 100 contiguous nucleotides of SEQ ID NO:1 and wherein expression of said nucleotide sequence suppresses gene expression which results in earlier flowering, or wherein said sequence comprises 100 contiguous nucleotides of SEQ ID NO:1.

11. Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Claims 7-8, 10, 14, 16, 20, 22-24, and 26-32 are not allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
March 16, 2004

PHUONG T. BUI
PRIMARY EXAMINER
3/17/04